The University of Arizona
Program in Applied Mathematics

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Greetings from the Chair, Applied Mathematics Steering Committee

Tim Secomb

Leadership of the Program

When Michael Tabor stepped down as Program Head, following more than two decades of dedicated leadership, a search committee was appointed to recruit a new permanent leader for the Program. This committee completed its review of applications and made its recommendations in mid-2016, but the chosen candidate eventually declined the position. The search committee has been reactivated and is considering several highly qualified potential candidates.

In the meantime, Moysey Brio was appointed as Interim Chair. The program has continued to flourish under his leadership. Recognizing the increasing demand for our graduates in the knowledge-based economy, particularly in industrial and governmental research, and the benefits of interdisciplinary research experiences, Dr. Brio has worked to develop partnerships with industry and with other departments. He has expanded the involvement of other Applied Mathematics faculty in the running of the program. These developments, combined with the excellent service provided by the administrative staff, Stacey LaBorde and Keri Oligmueller, have maintained and enhanced the effective running of the program.

During the spring semester of 2018, Dr. Brio will be on sabbatical leave, giving him a well-deserved opportunity to devote more time to his own collaborative research projects. On behalf of all involved in the Program in Applied Mathematics, I would like to express our appreciation for his great service as Interim Chair, which has, I am sure, extended for a longer period than he had originally expected.

I am pleased to announce that Janek Wehr, Professor of Mathematics, has been appointed as Interim Chair during Dr. Brio's absence, and thank him for his willingness to take on this responsibility. Dr. Wehr writes:

"I got my M.S. degree from the Department of Mathematics of Warsaw University. My main thesis adviser was Tadeusz Balaban, a world-class mathematical physicist. I pursued my interest in mathematical physics working on my Ph.D. with Michael Aizenman at Rutgers. For several years after that, in Princeton and later at the University of Arizona, I continued studying problems in theory of disordered systems. Beginning in 2004, I started working closely with physics groups, first with the quantum optics group of Maciej Lewenstein at the Institute of Optical Sciences in Barcelona, and then also with Giovanni Volpe, an experimentalist, now at the University of Gothenburg (Sweden). I am now working mostly on nonequilibrium statistical physics, classical as well as quantum. A part of my work is directly related to experiments; another part aims at applying quantum Langevin equations to describe open quantum systems. Recently, I developed an interest in mathematical biology. I am working on a model of gene expression with Jacek Miekisz at the University of Warsaw and initiating a collaboration with a neuroscience group at the University of Arizona Medical Center. At the heart of my daily activity is work with graduate students. Over the years I taught about thirty graduate courses and supervised Ph.D. dissertations of six students, of which three were in the Applied Mathematics Program. I want to continue this work and help the Program to maintain its high quality by leading it during the next semester."

On a personal note, the Program in Applied Mathematics has been a key part of my own academic life for many years. Thank you everyone associated with program, past and present – students, faculty, staff, donors, friends – for all your work and support. Please visit the new and improved website at http://appliedmath.arizona.edu/ for information, and enjoy reading this Newsletter.

Best wishes,
Tim Secomb
Chair, Applied Mathematics Steering Committee

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Michael Tabor Graduate Scholarship Award

Soon Hoe Lim, 5th Year Student

I would like to express my sincere gratitude and appreciation for the Michael Tabor Scholarship Award for the generous support that it has provided me for part of my journey in the applied mathematics PhD program at the University of Arizona. The scholarship has allowed me to fully concentrate on my research projects.

I am currently working under the supervision of Dr. Janek Wehr and we are collaborating with Dr. Maciej Lewenstein and members of his quantum optics group at the Institut de Ciències Fotòniques (ICFO) in Barcelona. My research focuses on multiscale reduction of noisy dynamical systems. Dynamics of many noisy complex systems, classical or quantum in nature, often exhibit one or more widely separated time scales. It is desirable to derive reduced, simplified models to gain deeper understanding of such systems. The main agenda in our research program is to derive and justify, starting from a microscopic model for the noisy system, an emergent macroscopic model that retains the essential dynamics characteristics of the degrees of freedom of interest (the slow variables) in the limit of infinite time scales separation. This falls under the umbrella of stochastic homogenization problems and may be studied using tools from stochastic calculus and insights from statistical physics.

A canonical model that we have been studying is classical Brownian motion in an inhomogeneous heat bath. Starting from models in the form of stochastic differential equations (SDEs), we study how inhomogeneity as well as noise spectrum of the heat bath influences the effective dynamics of the particle, in the limit when one or more characteristic time scales of the system tend to zero. In the so-called Smoluchowski-Kramers (or small mass) limit, the homogenized SDE of the particle's position contains interesting correction drift terms, the so-called noise-induced drifts, which have far reaching implications for many systems in statistical physics. For instance, our results can be applied to study systems of a single particle, of nanoscale, moving in a heat bath. In many cases, memory effects are present and the systems diffuse anomalously. Such systems are of particular interest in soft matter physics and nanotechnology.

Another part of our research program is about extending such studies to a model of quantum Brownian motion (QBM) in an inhomogeneous environment. A systematic study of the quantum noise-induced phenomena in the context of QBM is one of the principal challenges in our program. To carry out the quantum studies the technical tools needed are much richer. We need a noncommutative version of the stochastic calculus (quantum stochastic calculus of Hudson-Parthasarathy) and tools from operator theory. The studies for quantum systems at the low temperature regime is particularly important, but is much more intricate than the classical counterparts due to dominance of memory effects and the quantum nature of the noise. An instance of an open quantum system of interest which gains increasing attention in the fields of quantum optics and technologies these days is the system of a quantum impurity in Bose-Einstein condensates.

Although I have been particularly interested in problems arising in mathematics and physics, I do not identify myself purely as a traditional mathematician or physicist. I would like to think of myself as a scientist who is actively exploring new worlds. I believe that who you really are is at the heart of the science you are doing. I am passionate about developing and applying ideas and methods to understand and solve problems of interest arising in diverse fields, including mathematics and physics. I find that interdisciplinary research provides the best sets of problems and are also the most exciting to work on. It not only connects ideas from different fields and allows the rebirth of old ideas coming from other fields, but also encourages novel and creative ways of thinking about problems. It is my hope that the Michael Tabor Scholarship will continue to aid my development as a professional scientist for the rest of my PhD career.

New Program Affiliate Members

Calvin Zhang, Assistant Professor, Department of Mathematics

Calvin Zhang joined the faculty of the Department of Mathematics at the University of Arizona in 2016. He received his BS in Information & Computational Sciences from Zhejiang University in 2008. After earning his PhD in Applied Mathematics from UC, Davis in 2013, he worked as an Assistant Professor at the Courant Institute of Mathematical Sciences, NY.

My research is concerned with the mathematical aspects of biology. I use mathematics, physics and computing to study problems arising in neurophysiology at molecular, cellular and systems levels. I am also interested in various aspects of applied mathematics itself.

One of my recent research topics is in the modeling, analysis and simulation of synaptic transmission. A fundamental challenge in biology is to understand how the human brain works. Neurons form complex networks via synapses through which information propagate. Information transfer from one neuron to another occurs through a cascade of biophysical and biochemical processes, often stochastic in nature. A crucial step in this physiological process is the stochastic release of neurotransmitter vesicles. The probabilistic nature of vesicle release is one of the most significant sources of randomness in the central nervous system. Stochastic vesicle release affects information transfer from a presynaptic neuron to a postsynaptic neuron, and hence may play not only an important role in short-term plasticity but also a significant role in determining the functionality of certain synapses, the failure of which can lead to severe neurological disorders such as schizophrenia and depression.

It is commonly believed that stochastic vesicle release is an unwelcoming artifact of the nervous system and generally degrades the fidelity of synaptic transmission. To check the validity of this conjecture, Charles Peskin (Courant Institute) and I recently built a simple, microscopic model of the presynaptic vesicle docking and release processes. In this idealized model, neurotransmitter vesicles dock at the presynaptic terminal by a Poisson process with mean rate α_0. Upon the arrival of each nerve impulse, each docked neurotransmitter vesicle has a probability of p_0 to be released, resulting in an excitatory or inhibitory postsynaptic potential. To address how p_0 affects the fidelity of synaptic transmission, we used optimal linear filter theory to compute the optimal postsynaptic response. We found that as p_0 decreases, the mean square error in the estimation of various desired signals decreases monotonically. That is, a more stochastic release of neurotransmitters (a smaller p_0) leads to a more faithful synaptic transmission, whereas a deterministic release ($p_0 = 1$) leads to the least desirable outcome! (This result should be understood under the context that even at $p_0 = 1$, the model synapse is still stochastic since vesicle docking remains Poisson.) Therefore, the probabilistic nature of synaptic vesicle docking and release plays a beneficial role in synaptic transmission. More importantly, our recent results directly linked the stochastic nature of vesicle release to the functional role of the synapse, and showed that the size of the vesicle pool, vesicle docking rate and the release probability together play a dominant role in shaping the filtering property and the capacity of synaptic transmission.

More work need to be done to elucidate how various processes in vesicle dynamics influence the features and capacity of neuronal information processing at chemical synapses. Using mathematical equations that capture the essential deterministic and stochastic processes involved in vesicle dynamics, my research group will study how various sources of randomness in synaptic transmission affect information transfer in neuronal networks. I hope this work will provide insights and a systematic mathematical framework to elucidate the functional significance of stochastic vesicle dynamics in synaptic plasticity and neuronal computation. In addition, the mathematical models developed here can be extended or modified to incorporate biophysical details of other types of cells (e.g., immune cells, and hormone cells), and therefore highlighting general principles of vesicle fusion underlying distinct biological systems that exhibit exocytosis.

Alumni Profiles

Elizabeth Hunke (PhD 1994), Deputy Group Leader and Sea Ice Scientist, T-3 Fluid Dynamics and Solid Mechanics Group, Los Alamos National Laboratory

I am a senior scientist and the Deputy Group Leader of the T-3 Fluid Dynamics and Solid Mechanics Group at Los Alamos National Laboratory, where I've worked since finishing my Ph.D. I am the principal developer of the Los Alamos Sea Ice Model, CICE, which is used in numerous operational and climate modeling centers around the world, including the U.S. Navy, the U.K. Met Office, and the NCAR/DOE Community Earth System Model CESM. CICE was developed for global climate studies on highly parallel computing systems, and it is also used for smaller scale, higher resolution studies of regional climate processes. With its comprehensive physical sea ice representation and ability to produce realistic results on time scales from days to centuries, it is widely recognized as the leading sea ice model by the international Earth system modeling community. I was a contributing author for the Intergovernmental Panel on Climate Change (IPCC) Fourth and Fifth Assessment Reports, and I now lead the CICE Consortium, an international group of institutions jointly maintaining and developing CICE in the public domain for the research and operational communities.

I feel extremely fortunate to have quickly found a geophysical modeling niche at Los Alamos in which I could excel, but this was not pure luck — I have had the support of many mentors at all stages of my technical career.

One of my earlier math-related memories is of marching to the front of my 10th grade Algebra I class in a fit of pique, to show the teacher how to correctly solve a particular problem. He was a gym teacher and math was not his best subject. Remarkably, he was not offended (I was mortified afterward), and his positive reaction gave me some confidence that I could speak with authority on technical subjects. During my senior year of high school, my Algebra II teacher, Mrs. Orman, inspired me to explore mathematics more deeply during college. (My high school did not offer math courses beyond Algebra II.)

As an undergraduate student at Memphis State University, three professors, John Haddock, Don Francischetti, and Jim Campbell, introduced me to the world of higher mathematics, working with me on research problems in dynamical systems, random walk theory, and abstract algebra. I also spent a summer at AT&T Bell Laboratories working in Julia Phillip's molecular beam epitaxy lab, numerically simulating atomic bonds in a potential superconductor. Following her example, I decided that I wanted to work in a laboratory setting, and I realized that with a mathematics degree I'd have the basic skills to work on any scientific application that seemed interesting. I love the logic and elegance of mathematical theory, but I love it most when I can use it to address real-world problems. My MSU professors steered me toward the University of Arizona's applied mathematics program.

During my first year in Tucson, Alan Newell presented a mathematical description of how hurricanes work. I have always thought clouds were beautiful and mysterious, and my farming family depended on natural rainfall patterns, sometimes suffering through deluges brought by Gulf of Mexico storms. I was thrilled to study such a powerful aspect of the weather, and this topic became the focus of my graduate studies. I worked with Joe Zehnder in the Atmospheric Sciences department, with exceptional mentoring from two mathematicians, Mac Hyman and Dave Levermore. Mac

found a postdoc position for me with John Dukowicz and the ocean modeling team at Los Alamos National Laboratory, and he continues to be a bedrock of support for me as a scientist. Dave is like a guardian angel, his advice still audible in my head twenty-five years later. No less important were my classmates in the applied math program, who were awesome then and continue to hold my highest regard now. All of these people shaped my career and indeed my worldview.

I am fortunate: I learned to fly at Ryan airfield west of Tucson during graduate school. A few years later I spent 6 weeks on board a British navy vessel in the Weddell Sea, just off the coast of Antarctica. I've been to the Arctic more than once. I travel all over the world as a member of the International Arctic Science Committee. I've just been honored as a Rothschild Fellow of the Isaac Newton Institute for Mathematical Sciences at the University of Cambridge, U.K. But my greatest satisfaction derives from knowing that my work has made a positive difference. For instance, a few years ago an unusual, early storm prevented the final fuel shipment from reaching Nome, Alaska before winter. Sea ice packed in along the coast and the town was going to run out of fuel in March. Using the Navy's operational forecasting model, which includes CICE, a U.S. Coast Guard icebreaker guided a Russian tanker through 300 miles of ice to deliver 1.3 million gallons of fuel. That, alone, has made my career worthwhile.

Although we admire successful people around us, the process of getting there is often the most inspiring part of their stories — and ours. Mary Hockaday, a senior manager at LANL, gave a sage piece of advice: be a mentor, and have a mentor, no matter your age or status. Mentoring makes a huge difference in people's lives.

Alumni Profiles *(continued)*

Arthur Lo (PhD 2004), Associate Director in Drug Metabolism and Pharmacokinetics Dept., Theravance Biopharma Inc.

Math combined with something else was a consistent thread for me through undergraduate and graduate school. During my undergraduate studies, it was indecision on my part to avoid committing to a single field of study, so I continued to take math classes along with other classes in physiology and economics. When exploring options for graduate school, there were a few schools with interdisciplinary programs in mathematical biology or mathematical finance, but acceptance was also a commitment to the individual program and a specific advisor.

Conveniently, the Program in Applied in Mathematics had no requirement for specifying a field of research until after the qualifying exams. After the first year was completed and if we were able to pass the qualifying exam, we could investigate all avenues for research. It was an appealing option to take additional time to explore other disciplines prior to committing to a single area of research.

The first year was a high hurdle to complete, even though I was also fortunate enough to receive a Flinn Fellowship for the first year to offset the need to teach. There really weren't any excuses for not focusing on the core classes, but the concepts that were presented in Principles of Analysis were hard to grasp when my strengths were around applying the appropriate analytical techniques to research problems. Dr. Tabor did point out that "when someone sees that your degree is in applied mathematics, they will expect that you have knowledge of mathematics." Eventually, someone was sufficiently persuaded that I had enough mathematical knowledge to avoid embarrassing the program too much.

The biomath seminar was a good introduction to interdisciplinary research, bringing together various students and faculty from across campus who had an interest in combining mathematics and biology. Students from evolutionary biology and ecology, physiology, pharmacology, biomedical engineering, astronomy and others attended the seminar and gave joint presentations to help foster interactions across the departments. It was a great concept to show the wide variety of interdisciplinary research at the university and to demonstrate the applicability of mathematical approaches in research. The interactions with students from the other departments provided ample opportunities to see different viewpoints for approaching research problems; though it was sometimes difficult to be excited about flagellar propulsion or beetle population dynamics when my focus has been more toward physiological systems. The seminar was also my first introduction to pharmacokinetics, even though the use of ordinary differential equations to describe plasma drug concentrations struck me as relatively simplistic at the time.

I also managed to explore other disciplines outside of physiology, including taking core classes in economic systems design with future Nobel Laureate Vernon Smith. It was a great opportunity to learn about auction design theory and experimental economics, and to approach the economics research from a mathematical viewpoint. Again, it was enlightening to see how students from different backgrounds approached the same problems in class.

Alumni Profiles (*continued*)

After some wandering, I returned my focus to human physiology and spent my time in Tucson working with Dr. Timothy Secomb on the diffusion of oxygen from capillaries to working muscle in the context of matching vascular recruitment to muscle fiber activation. We worked to describe how the pathways for the regulation of blood flow and oxygen delivery were matched to the regulation of muscle activity and corresponding oxygen consumption within the geometry of the muscle. The bigger goal was to evaluate the disruption in the system when the regulatory pathways were altered due to injury or age. The best part of the work was explaining the math to the non-mathematicians, and explaining the physiology of the microcirculation and neuromuscular pathways to those who were not life scientists.

My choices for employment following graduation were mostly academic in nature - Dr. Secomb's standing in the research community lead to multiple opportunities for postdoctoral research across the country. Similarly, my interactions during the summers at Los Alamos also provided a chance to conduct research at the National Lab. Instead, I remembered two early employees from a small company who attended a summer course in nonlinear dynamics in physiology at McGill.

The company was Entelos, and they were building large systems of ordinary differential equations to represent the behavior of physiological systems. The goal of the company was to use mathematical modeling approaches to help drive better decision making in the pharmaceutical industry. If the aerospace industry was using modeling and simulation to build airplanes, then the same approaches could also be used in the pharmaceutical industry. It was an application of mathematics to physiology that required interdisciplinary collaborations between scientists.

Entelos had core models built that represented Type 1 and Type 2 diabetes, rheumatoid arthritis, asthma and other therapeutic areas, with which they tested the effects of novel therapies that were implemented as perturbations to the model. In the model of human metabolism built to represent the pathophysiological changes in glucose handling leading to elevated glucose levels in the blood (Type 2 diabetes), the daily cycle of food intake in the form of carbohydrates, protein and fat was tracked from intestinal absorption into the systemic circulation, to storage in the liver, adipose tissue and muscle, and to consumption by daily activity. The mass balance of glucose could be followed, from the amount generated by the breakdown of carbohydrates, to the amount transported into liver and muscle and converted to glycogen. Similarly, the amount of glycogen converted to glucose and consumed by the Krebs cycle to provide energy could be quantified. Changes to the set points of certain glucose pathways in response to insulin would alter the model behavior, leading to changes in the levels of circulating glucose.

Each model was continuously developed to incorporate the required physiological pathways that were of interest to the clients, who were a mix of large pharmaceutical companies and FDA collaborations. As each model was modified, the core behavior of the model needed to remain the same with the prior functionality and dynamic behavior intact. The effects of a new therapy that decreased liver uptake of glucose could be parameterized as a direct effect on the rate of hepatic glucose uptake, but that effect could not alter the secondary response of the liver to other perturbations such as a fast or an injection of insulin. Changes or additions to the model were necessarily constrained by human physiology and pathways at steady state and the response to the known effects of existing therapies or other interventions.

The entire approach is sound, but legacy model behavior becomes increasingly difficult to maintain as the models become more complicated with increasing feedback loops. Small and large changes to states and parameters in the system of ODEs needed to be done in a manner that best represented the known biology, which meant determining how the implementation of the changes could be done to such that certain states were minimally affected. The common approach was to target the changes in states and parameters to areas in the model where there was the greatest physiological uncertainty based upon the data in the literature, or where sensitivity analyses suggested parameters would have the least impact on global behavior. Larger changes required more work to effectively implement new model behaviors while maintaining legacy behavior. A close collaboration between the scientists was required to complete the changes to the model within a timeframe to answer pending questions from the client and to simultaneously satisfy the client that the correct physiology was represented in the model.

While the underlying relationships of physiological systems and pathways were represented by a single model structure, the parameters describing the model were not necessarily unique. Entelos leveraged the identifiability problem by creating a multiple parameterizations of the model, termed "virtual patients", to represent the diversity of human physiology. Virtual patients could have increased food intake that could be offset by increased basal metabolic rates due to increased muscle mass and greater aerobic activity, or patients with normal food intake could have decreased activity levels leading to greater storage of excess glucose in the adipose tissue. Both situations result in increasing body weight. The variability in the underlying physiology lead to variability in the response to perturbations of the system, ideally resulting in a better ability to estimate the range of responses to the perturbations and potentially leading to methodologies for identifying and stratifying patients that may respond better or worse to specific therapeutic targets.

Entelos also developed infrastructure and software to handle collaborative model development and maintenance.

The in-house software provided a visual interface to view and easily modify the relationships between model states, manage different parameter sets, and automatically provide validation checks on model behavior and states to manage responses to model perturbations. As the combinatorics of model structure and behavior were addressed by the software, a backend database was used to store and synchronize simulation results to allow multiple people to collaborate on the same model, and a compute cluster was built to offload the simulation of the large system of equations over the range of virtual patients. It was a soup to nuts system for developing large models that helped introduce the ideas of quantitative systems physiology to the pharmaceutical industry.

Even though the methodology and the science were reasonable, a commercial business doesn't work if there are no clients to pay for the work, nor scientists to conduct the work. Research consulting development typically involved scientists modifying the parameters and equations to address research questions, but other core scientists were required to continue model development while programmers were required to maintain the computational infrastructure. This resulted in a consulting model where higher fees were required to sustain the large overhead leading to a limited pool of potential customers who could afford the investment. Similarly, finding scientists with the ability to comb through research papers across a wide array of physiological systems, implement their findings using differential equations, and effectively present results to pharmaceutical scientists and clinicians was more difficult a decade ago than it is now. The applicant pool consisted of graduate students in certain quantitative fields, and biological scientists with a mathematical inclination, which resulted in higher than typical salary costs.

Unfortunately, Entelos didn't survive the combined storms of the financial crisis in 2008 and management's ambition to expand the business into new opportunities away from the core competencies of the company. The money coming in has to be greater than the money going out at some point, and when it isn't, the costs of borrowing money during a financial crisis are often unfavorable lending terms. The process of going through the layoffs, bankruptcy, management and ownership turnover resulted in another education into the business aspects of scientific research consulting.

Although the company has been relegated to history, its former employees and methodologies continue to be used for pharmaceutical research. The application of a dynamical systems approach for the representation of disease pathophysiologies continues to impact decision making at pharmaceutical and governmental organizations. One of the original developers of the human metabolism model, Kevin Hall, is now at the National Institutes of Diabetes and Digestive and Kidney Diseases applying mathematical models to study metabolism and body weight regulation. The cardiovascular model for atherosclerosis was brought into the FDA for their evaluation. A model for blood pressure regulation and hypertension is being used to investigate therapies for renal disease. Even features from Entelos' software have now been incorporated into more broadly available programs, such as the Systems Biology Toolbox in Matlab.

I've been fortunate to join other former colleagues in finding a job within the pharmaceutical companies themselves, providing the same type of analyses without the added layer of being a consultant. Cecilia Fosser (2000) at Cytel and Katherine Williams (2016) at Applied Biomath are two other Applied Math graduates who are also in the same line of work today, utilizing mathematical approaches to help answer questions, identify novel targets, and guide decision making in the pharmaceutical industry. The work ultimately simplifies down to using the most efficient mathematical approaches for addressing questions that arise during the course of drug development. The math isn't overly complicated or challenging, but the challenge arises in making a compelling case with supporting evidence to non-mathematicians for why a decision on clinical research or development should be made one way or another.

Current Student Profiles

Victoria Gershuny (4th Year Student)

My grandmother is a doctor of internal medicine and I have always looked up to her. At four years old, I had learned how to measure blood pressure with her guidance, and because of the example she set for me, in elementary school, I was inseparable with an anatomy textbook. Since those days, I have realized that what I admire most about my grandmother, is not her role simply as a doctor. Rather, her ability to creatively problem solve, application of external studies to aide patients in overcoming illnesses, and perpetual quest for knowledge are all of the characteristics that I too hope to develop.

What could I do in college to find myself in the person I aspired to be? I tried everything from volunteering at a hospital, to dancing for the University of Colorado Buff Gold Dance team, to interning as an engineer. However, I didn't find my true passion until I took up a professor on an offer to do some math research over the summer. Granted, all I did that summer was use that professors' undergraduate research funding to learn how to use MatLab, but it was through that experience that I fell in love with the world of mathematical biology. One of the first actual research projects that I took part in was in an REU program through the Math Biology Institute at the Indiana University-Purdue University at Indianapolis. I worked with a team to model autoregulation of retinal blood flow in patients with glaucoma. My part of the research looked at the retinal tissue Carbon dioxide concentration, as it affects the dilation and constriction of the arteries and tissues in the retina and identified that mechanism to be very significant. The use of mathematics to help understand diseases and their treatments is something I have since then, only grown to enjoy more.

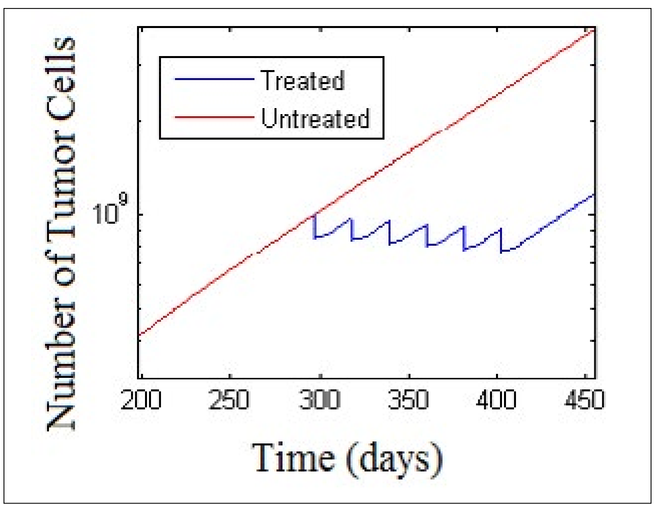
For my graduate work here at the University of Arizona, I am modeling tumor-immune interactions in the context of chemotherapy under the guidance of Tim Secomb and Ardith El-Kareh. Although specific treatments targeting the immune

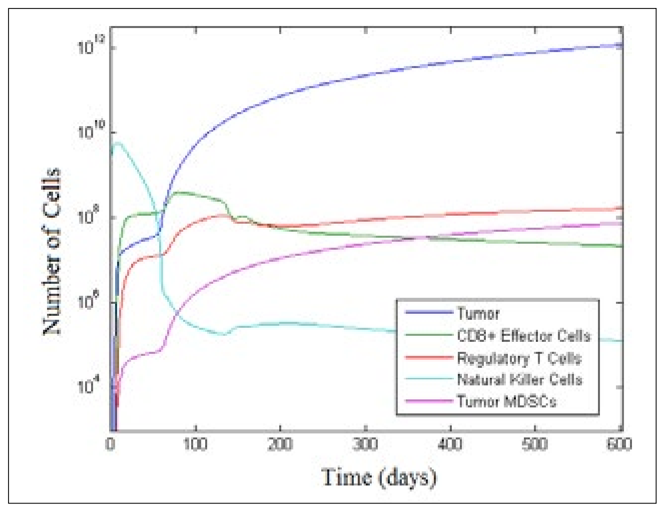
Current Student Profiles *(continued)*

system have only been developed recently, many standard chemotherapies are now known to have a strong immune effect. One such treatment, is the drug combination FOLFOX (5-fluorouracil, oxaliplatin and leucovorin) which is in wide clinical use for colorectal carcinoma. My research goal is to determine what the importance of the immune system is in this drug treatment and to find what schedules, dosing, and combinations with immunotherapy, would best utilize the immune system to eliminate tumors.

In the human body CD8+ Effector T cells and Natural Killer (NK) cells are the two key immune cell fighters of tumors. These alone, should have the capacity to eradicate and control the tumor, however, tumor cells and their microenvironment have an ability to suppress the immune response. One of the mechanisms by which they do that is by recruitment and stimulation of suppressive immune cells, such as regulatory T-cells and myeloid-derived suppressor cells (MDSCs). To understand the complex interplay between therapy, the tumor, and the immune system, I developed a model comprised of 17 coupled nonlinear ordinary differential equations. A substantial part of my project has been estimating parameters from experimental data and comparing the model's predicted cell counts and plasma levels over time to experimentally measured values in human patients. Using this model, I was able to find that for a single tumor nodule, the immune effects of oxaliplatin lead to an almost negligible increase in patient survival, however, the effects of 5-fluorouracil on the immune system are immense.

Through my research, I can resolve medical questions that cannot be studied experimentally and tease out the relative importance of different mechanisms. In the future, I hope to extend these skills to working for a pharmaceutical company and use similar models to help drive actual drug development. Like my grandmother. I hope to be at the forefront of fighting disease, but instead of a stethoscope, the tool I will use is math.





Ammon Washburn (4th Year Student)

I was at a crossroads in my life. I was working at a local start-up and they mentioned several times that they would be interested in hiring me full time. Even saying they would be willing to pay my health insurance for my new baby if I promised to stay. On the other hand I was accepted into the University of Arizona's applied math PhD program and I had always wanted to go to graduate school. After careful deliberation I decided I wanted to know why and not just how.

After having a normal challenging first year, I met Neng Fan of the Systems and Industrial Engineering department during a seminar where potential advisers from across the campus can recruit from applied math graduate students. He has been a great adviser who has taught me a lot and let me take my own direction even when funding wasn't necessarily there.

In a way I have come back to where I was long ago at that cross roads. I now deal with large amounts of data trying to gain some insight that will help others. However instead of helping companies gather data on their competitors, I now analyze cancer.

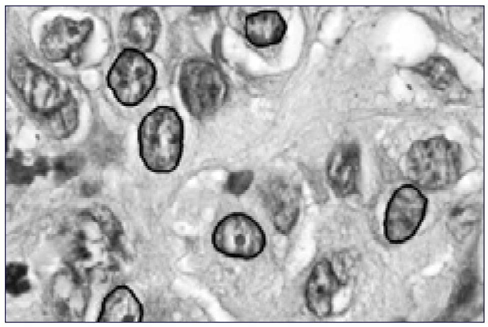
Current Student Profiles *(continued)*

Specifically I work with karyometry data which comes from analyzing images of cell nuclei. With these images we hope to unlock the secrets of a tricky variant of pancreatic cancer called intraductal papillary mucinous neoplasm. I modify existing machine learning methods to deal with the inherent challenges of working with this data.

I also have a love of understanding the mathematical and statistical theory behind machine learning algorithms. I have tried to understand the model behind each method and why it is successful. I have been able to generalize many of their good properties and also develop a quick algorithm to tune it properly.

My family have loved our time in Tucson. Some of our highlights are hiking the seven falls, camping on top of Mt Lemmon, and going to see the free raptor flight at the Desert Museum. We love dancing in the monsoon rain, hiking in the middle of December and being able to go to the playgrounds all year round.

This is most likely my last year here and it makes me sad because I have had the opportunity to learn so much. I have gone to the University of Washington for their summer institute in big data for statistics, presented at conferences in Nashville, TN and Houston, TX, and just barely did an internship at Los Alamos National Labs. This blending of learning and practicing will help me throughout all my life.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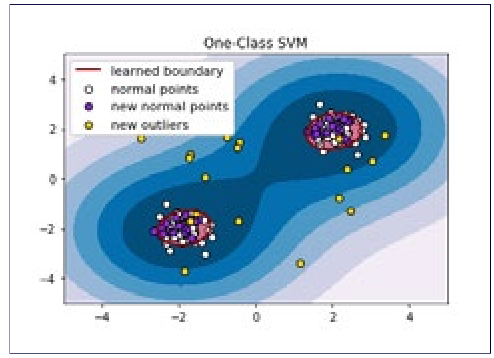


News from Members and Affiliates

Jim Cushing (Mathematics): I chaired the organizing & scientific advisory committees for the Sixth International Conference on Mathematical Modeling and Analysis of Populations in Biological Systems (ICMA-VI) held October 20 - 22, 2017 in the new ENR2 building on campus. Local members of the organizing committee were Joceline Lega and Joseph Watkins. This was the sixth in a biannual conference which started twelve years ago here at the University of Arizona. The conference hosted about 140 participants including 5 plenary and feature lecturers, 78 contributing speakers, and 35 poster presenters. Participants came from Canada, Europe, Africa, and India. The general theme of the ICMA conferences is the analysis of mathematical models for the temporal dynamics of biological populations. A special emphasis at the sixth conference was placed on the effects of environmental/climate change. Specific topics include, but were not limited to: Population & ecological dynamics, Adaptation & evolutionary dynamics, Dynamics of infectious diseases, Dispersal and distribution of populations, Invasions and endangered species, Management of natural resources

Jean-Marc Fellous (Psychology): Publications: Lines, J., Nation K. and Fellous JM. Dorso-Ventral and Proximo-Distal Hippocampal Processing Account for the Influences of Sleep and Context on Memory (Re) consolidation: A Connectionist Model. Computational Intelligence and Neuroscience. In press, 2017. Gianelli S., Harland B. and Fellous JM. A New Rat-Compatible Robotic Framework for Spatial Navigation Behavioral Experiments. Journal of Neuroscience Methods, In press, 2017. Grant: Dr. Jean-Marc Fellous has been awarded a 4 year NSF grant to study the neural mechanisms of complex spatial navigation. The project will involve state of the art wireless and optogenetics methods, and the study of multi-scale spatial coding. They will use new computational techniques to assess

News from Members and Affiliates (*continued*)

the efficiency of the spatial code, and in collaboration with the University of South Florida, the project will also involve multi-scale spatial navigation in autonomous mobile robots.

Joceline Lega (Mathematics): Honors: Elected Fellow of the American Association for the Advancement of Science, 2017 Publications: N.M. Ercolani, N. Kamburov, J. Lega, The Phase Structure of Grain Boundaries, to appear in Philosophical Transactions of the Royal Society A J. Lega, H.E. Brown, R. Barrera, Aedes aegypti (Diptera: Culicidae) abundance model improved with relative humidity and precipitation-driven egg hatching, J. Med. Entomol. 54, 1375–1384 (2017) H.E. Brown, R. Barrera, A.C. Comrie, J. Lega, Effect of temperature thresholds on modeled Aedes aegypti population dynamics, J. Med. Entomol. 54, 869–877 (2017) Invited talks: The phase structure of grain boundaries; Special Session on Nonlinear Waves: Analysis and Numerics, 1126th AMS Meeting, College of Charleston, Charleston, SC, March 10-12, 2017 The phase structure of grain boundaries; Applied Mathematics Colloquium, IIMAS, Universidad Nacional Autónoma de México, Mexico City, Mexico, April 19, 2017 15. Three models to help understand the spread of mosquito-borne diseases; 10th IIMAS Colloquium, Universidad Nacional Autónoma de México, Mexico City, Mexico, April 20, 2017. Patterns, defects, and phase singularities; Plenary talk, Rocky Mountain Partial Differential Equations Conference, Provo, UT, 18 – 19 May, 2017. The Phase Structure of Grain Boundaries; Session on Spatiotemporally Complex Patterns, 2017 SIAM Conference on Applications of Dynamical Systems, Snowbird, UT, May 21 – 25, 2017. Forecasting the Flu with Simple Nonlinear Models; Seasonal Influenza Forecasting Workshop, Centers for Disease Control and Prevention, Atlanta, GA, August 28 – 29, 2017. A Three-pronged Approach to Predicting the Spread of Mosquito-borne Diseases; Mathematics Colloquium, Colorado State University, CO, November 13, 2017.

Joanna Masel (Ecology & Evolutionary Biology) Publication: "Intercellular Competition and Inevitability of Multicellular Aging," published in Proceedings of the National Academy of Sciences, Paul Nelson and Joanna Masel. A mathematical proof that aging is an inevitable result of multicellularity, published in PNAS. https://www.eurekalert.org/pub_releases/2017-10/uoa-imi102717.php

Recent Graduates

Michael Borghese (PhD 2017) Currently working as a Data Scientist for the Honest Co., Los Angeles, CA.

Isak Kilen (PhD 2017) is currently working as a postdoctoral research associate in the College of Optical Sciences at the University of Arizona. The research, an extension of his thesis projects, involves numerical simulation and modeling of microscopic non-equilibrium dynamics in semiconductor disk lasers. His day job is solving complex problems alongside an international interdisciplinary group of theoretical physicists, mathematicians, optical engineers, and material scientists. At night, he loves to play with puppies and kittens.

Andrew Leach (PhD 2017) Currently working as a Machine Learning Deployment Engineer at Google, Mountain View, CA.

Erica McEvoy (PhD 2017) Accepted to the Insight Data Science Fellowship program in San Francisco, beginning in January, 2018.

Emily Meissen (PhD 2017) Currently working as a Business Data Analyst for Intuit, Tucson AZ.

Toby Shearman (PhD 2017) Currently working as a Data Scientist, Conversant LLC, Chicago, IL.

Alex Young (PhD 2017) Recently began a postdoctoral research position at Duke University. He is working with an interdisciplinary group of statisticians and applied mathematicians investigating techniques to accelerate sampling for Bayesian posterior inference. Additionally, Alex is working on a pair of projects centered on Bayesian modeling under geometric and probabilistic constraints.

News from Alumni

Julia Arciero (PhD 2008) received an NSF CAREER Award entitled "CAREER: Integrating theory and experiment to assess the contribution of distinct vascular segments in arterial insufficiency" This award is for 2017-2022. She was tenured and promoted to Associate Professor this year.

On Friday, November 10, 2017 we hosted Dr. Timothy Secomb at IUPUI (Indiana University - Purdue University Indianapolis) and he gave the Math Department Colloquium Talk. This was an especially nice event, since Tim was both Julia's PhD advisor and **Jared Barber's (PhD 2009)** advisor, and now both Jared and Julia are faculty members in the Department of Mathematical Sciences at IUPUI.

Richard (Rick) Brazier (PhD 1997) was recently promoted to Professor of Mathematics and Geology and also officially started his role as Senior Associate Dean for the Commonwealth Campuses of Penn State University.

Daniel Coombs (PhD 2001) is getting increasingly involved in microscopic imaging of cells. This year, with the team at UBC, he published a paper on single molecule tracking on B cells (citation below) and is now working hard on new methods for analyzing super-resolution optical microscopy. He is also looking forward to a sabbatical year in 2018-2019.

Cecilia Fosser (PhD 2000) is the Director, Head of Quantitative Pharmacology and Pharmacometrics and Phase 1 Biostatistics at Cytel. Leads a global group that performs 4 distinct functions: 1). Pharmacometrics 2). Quantitative Pharmacology including Non-Compartmental Analysis (NCA) 3). Phase 1 Biostatistics 4). Creation of Comparator Databases. In addition, provide model informed drug development consultation and perform exposure-response modeling and simulation of pre-clinical and clinical data, including translational modeling and model-based, meta-analysis.

Kevin Gross (PhD 1999) 2017 has been an exciting time with the launch of the dual-camera systems on the iPhone 7+, 8+ and the imminent launch of the iPhone X, we've successfully brought computational photography to the consumer market with the Portrait Mode feature. This feature simulates a shallow depth of field (similar to a large-aperture lens on a SLR camera) by rendering an image with a stereo-depth-based bokeh that is ideal for portrait photography. Kevin's contributions include: developing mathematical models of the lenses which are optically inspired and go far beyond pinholes or other "thin lens" approximations, developing optimization algorithms and test setups to estimate the parameters of our lens models, bringing up factories across the globe to build and calibrate the cameras, leading and contributing to a cross-functional team of hardware, software, firmware and silicon design engineers to realize the feature. A busy year indeed. 2018 will be busier! Cheers!

Elizabeth Hunke (PhD 1994) was honored as a Rothschild Fellow of the Isaac Newton Institute for Mathematical Sciences at the University of Cambridge, U.K.

William Johnson (PhD 1978) took a break from retirement by spending the 2016-2017 academic year as a visiting assistant professor at New Mexico Tech where he taught Calc I and III. He still works with friends on some papers and had two accepted on the same day. He also will be doing some consulting at Sandia National Laboratories this year.

Quintina Jones (MS 2010) was selected for the Chief Engineering Development Program; became the Project Lead for an Affordability Initiative using Model Based Engineering for cost reduction activities; received Engineering Technical Honors and multiple awards for efforts supporting multiple programs as a Technical Lead. She also passed her Comprehensive Exams for her PhD in Systems and Industrial Engineering with a minor in Applied Mathematics at the University of Arizona and advanced to Candidacy.

David Kopriva (PhD 1982) retired from FSU in May, 2017 but is still going to be busy. Beginning in June, 2017 he'll be teaching a course in Spectral Methods at the IIT Bubaneshwar as part to fifth Indian Government GIAN (Global Initiative of Academic Networks) program. He'll also use his Simons travel grant to continue collaboration in Germany and Spain on the development of Spectral Methods for fluid dynamics application. The program at the UofA was great, and put me on the right path for the next 30+ years. Also, a special issue of Computers and Fluids was organized to honor his 60th birthday: http://www.sciencedirect.com/science/journal/00457930/139

Andy Linfoot (PhD 2006) took a position at Microsoft and was one of the key contributors for Azure Machine Learning. He has a few patents and applications resulting from that work. The URL is https://azure.microsoft.com/en-us/services/machine-learning-studio/ He leads the infrastructure and runtime team that with the help of a couple other teams launched version 1. After that he did a lot of work getting the next major offering in the Machine Learning space together for Microsoft. The Azure Machine Learning Workbench can be found at http://azureml.azureedge.net/content/apphome/index.html

Having spent the last few years working in commercial/technical software development, he decided to try his hand in the Finance industry. So this past June, he left Microsoft and took a position at a Hedge Fund called Cargometrics. It has been interesting so far and he says as usual a lot of the things he learned in the Program have come in handy.

Shi Jin (PhD 1991) is currently Vilas Distinguished Achievement Professor at University of Wisconsin-Madison, and has been invited to give a 45 minute lecture at the International Congress of Mathematicians (ICM), to be held in Rio de Janeiro, Brazil, in August 2018. He will speak at the joint sections of Numerical Analysis and Scientific Computing, and Mathematics in Science and Technology.

Hayley (Miles-Leighton) Milbourne (MS 2013) is currently finishing her PhD in Mathematics Education at a joint program through San Diego State University and UC San Diego. She has been conducting research on ways to support high school english language learners with their mathematics courses and on the ways in which graduate teaching assistants make sense of and learn how to teach in a student-centered classroom. She runs and teaches the professional development in the Mathematics department at SDSU and is currently on the job market.

Marcel Oliver (PhD 1996) has been involved in the preparation of a major collaborative research network "Energy Transfers in Atmosphere and Ocean" and currently serve on its scientific steering committee, see http://www.trr-energytransfers.de/

The network consists of research groups from three German universities and five research institutes. It focuses on improving our understanding of the energy pathways between waves, eddies and local turbulence in the ocean and the atmosphere, with a view toward developing energetically consistent models to enhance the accuracy of climate analysis and climate predictions. The network connects oceanographers, atmospheric scientists, and mathematicians with research ranging from mathematical foundations, numerical analysis, high-performance computing to observational projects. The network is funded by the German Research Foundation with an initial budget of almost 10M Euro over four years, with possible extension for up to 12 years total. The interdisciplinary aspect of the network is very reminiscent of the spirit he experienced as a student in the Program in Applied Mathematics, and this experience was tremendously helpful during the preparatory phase.

James Powell (PhD 1990) took a leave of absence from Utah State University to serve as Program Director in Mathematical Biology, DMS, at the National Science Foundation in Alexandria, VA.

Edward Soares (PhD 1994) lead the effort to create a minor program in Statistics at Holy Cross and this year's graduating class will include the first statistics minors in the school's history. He began collaborative research with Prof. Beth Landis from the Department of Chemistry, in her work involving the analysis of nanoporous gold and is continuing work with Professor Amber Hupp (Department of Chemistry) in involving the analysis of biofuels. He is on sabbatical this year, working at Olin College of Engineering in Needham MA, continuing the above work. He is also working on some consulting projects with inviCRO, LLC with. Jack Hoppin (PhD 2003), co-founder and CEO. He plans to spend more time surfing all fall, winter and spring!

Guillermo Uribe (PhD 1993) is working as a data scientist for the Math department, University of Arizona. He developed a data mining algorithm to identify potential candidates to the major or minor among currently enrolled students; also developed a quick system to provide feedback to students after midterms for large multi-section courses; analyzing data on success of the current math placement policies and also contributes with teaching Math courses and advising students.

Current Student Achievements

J. Ruby Abrams (1st Year) published a paper in the SIAM Journal this semester titled Analysis of Equity Markets: A Graph Theory Approach. Here's a link to the site and the paper: http://www.siam.org/students/siuro/vol10/S01563.pdf

Jesse Adams (5th Year) attended the SIAM CSE in Atlanta, with travel funded by my internship and presented the poster "A numerical method for high energy x-ray source shape reconstruction". In the summer, I attended the MATRIX Institute conference and workshop on Computational Inverse Problems in Australia, with travel funded by the conference and gave a talk titled "MCMC-based deconvolution with reduced boundary artifacts and non-negativity constraints". I continued my internship at the Nevada National Security Site this summer. My advisor Matti Morzfeld submitted the paper "Feature-based data assimilation in geophysics" to the Journal Nonlinear Processes in Geophysics, for which I am a co-author. It is currently under review.

Patrick Greene (7th Year) was awarded $500 from the Don Wilson Applied Mathematics Fund to present a poster at the Society for Neuroscience Annual Conference in Washington, DC in November, 2017. The title for the poster is "Simultaneous spike sorting and source localization." I'll be presenting my work on a data analysis algorithm that I've developed with my advisor Kevin Lin. The algorithm uses a biophysical model to help determine neuron positions around a recording site and separate signals from noise. On October 11-14, 2017 I attended the Biomedical Engineering Society Annual Conference in Phoenix, AZ. I gave a presentation on optimal probe design for signal localization in neural recordings. On May 31, 2017 I attended the Eighth International Workshop on Statistical Analysis of Neuronal Data at the University of Pittsburgh in Pittsburgh, PA. I presented a poster about the statistical methods used in the spike sorting algorithm that my advisor and I have developed. The trip was funded through the NIGMS Training Grant: Computational and Mathematical Modeling of Biological Systems.

Travis Harty (4th Year) was awarded $500 from the Don Wilson Applied Mathematics Fund to present a poster at the American Geophysical Union Fall meeting in New Orleans, LA in December, 2017. The title of the poster is "Forecasting Global Horizontal Irradiance Using the LETKF and a Combination of Advected Satellite Images and Sparse Ground Sensors." The research is useful for forecasting solar power output.

Nicholas Henscheid (6th Year) presented a talk at the 6th Workshop on Computational Human Phantoms, Annapolis MD, August 2017. Presented a talk at the Texas Applied Mathematics and Engineering Symposium, Austin TX, Sept 2017. Received a travel award from organizers. Presented a poster at the IEEE Medical Imaging Conference, Atlanta GA, October 2017.

Andrew Hofstrand (5th Year) received an ARCS Foundation Scholarship for 2017.

Brian Hong (5th Year) presented ongoing research at the BMES Conference in October "A Unified Approach for Reconstructing Left Ventricle Kinematics from Noninvasive Imaging Data." Presented a poster at the Cardiac Physiome in November, 2017 in Toronto, CAN "An Efficient Computational Model for Left Ventricular Dynamics", received $500 funding from the Don Wilson Applied Mathematics Fund. Published a conference paper at the Large-Scale Scientific Computing conference "Towards a Scalable Multifidelity Simulation Approach for Electrokinetic Problems at the Mesoscale." Hong, Brian, Mauro Perego, Pavel Bochev, Amalie Frischknecht, and Edward Phillips co-authored an article in Cardiovascular Engineering and Technology "Simulation of Left Ventricular Dynamics Using a Low-Order Mathematical Model." Moulton, Michael J., Brian D. Hong, and Timothy W. Secomb. Collaborated with members of the Center for Computing Research at Sandia National Lab during a summer internship. Received an ARCS Foundation Scholarship for 2017.

Soon Hoe Lim (5th Year) was the Galileo Circle Scholarship recipient for Applied Mathematics.

Toby Shearman (PhD 2017) gave the annual Al Scott Lecture in April, 2017.

Craig Thompson (1st Year) presented a poster in October, 2017 at the ICMA VI conference titled "A new gravity model for spatial interaction: An application to highway flow estimation in the western United States".

Ammon Washburn (4th Year) attended Los Alamos National Labs for their Applied Machine Learning Internship summer 2017 in Los Alamos, NM. Presented at the INFORMS conference in Houston on October 23rd, 2017 titled, "Distributionally-robust CVaR Formulation of SVMs Using Wasserstein Metric" and received a GIDP - Carter Travel Award for this conference.

Zhuocheng Xiao (2nd Year) published a paper from my undergraduate years in Physical Review E., Title: "Cusps Enable Line Attractors for Neural Computation" Zhuocheng Xiao, Jiwei Zhang, Andrew T. Sornborger,* and Louis Tao; https://link.aps.org/doi/10.1103/PhysRevE.96.052308

The Don Wilson Applied Mathematics Endowed Fund for Excellence

The Don Wilson Applied Mathematics Endowed Fund for Excellence *was established to honor the memory of Don Wilson, a University of Arizona Research Professor in the College of Optical Sciences, with the purpose of providing support for the professional development of graduate students in the Program in Applied Mathematics. Dr. Wilson worked very closely with Harry Barrett's renowned medical imaging group and helped train many of the Applied Mathematics students who worked in that group. One of those students,* ***Jack Hoppin (PhD 2003)****, and his wife Janna Murgia, made a generous gift to the Program that enabled the fund to be established.*

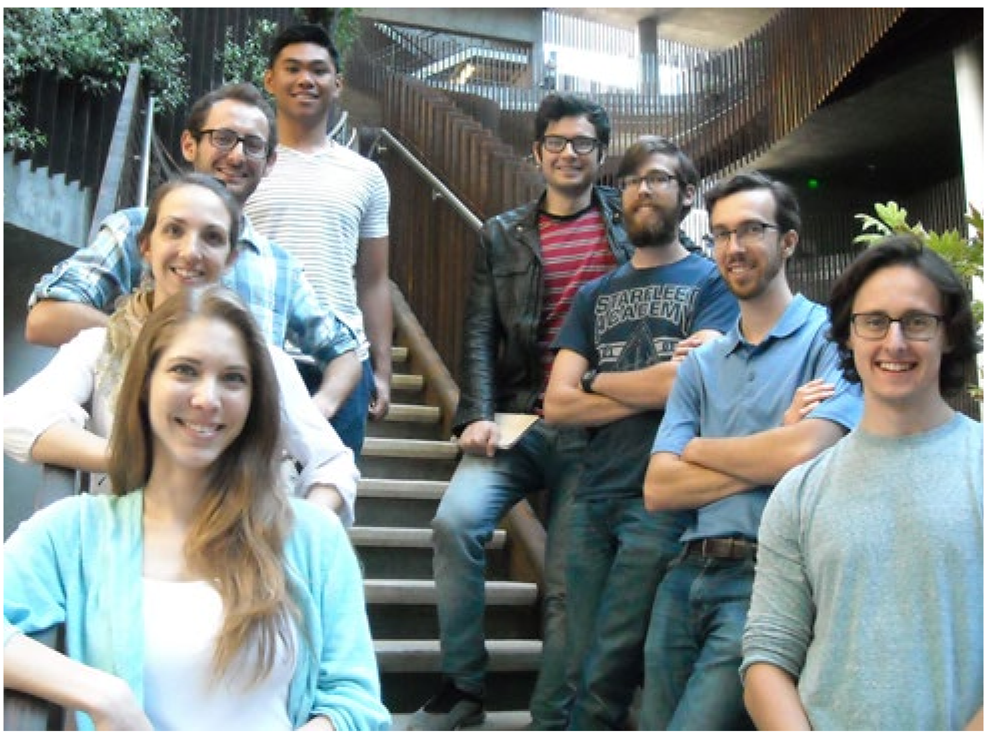
2017 Don Wilson Fund Recipients:

Patrick Greene (7th year student) was awarded $500 to present a poster at the Society for Neuroscience Annual Conference in Washington, DC in November, 2017.

Travis Harty (4th year student) was awarded $500 to present a poster at the American Geophysical Union Fall meeting in New Orleans, LA in December, 2017.

Brian Hong (5th year student) was awarded $500 to present a poster at the 2017 Cardiac Physiome Workshop in Toronto, Canada in November, 2017.

New Students Fall 2017



Incoming class, August 2017

from top left:

- **Jeffrey Lee**, CalPoly, San Luis Obispo
- **Joshua "Ruby" Abrams**, University of Arizona
- **Kim Sommerkamp**, Lindenwood University
- **Kathryn Stefanko**, Arizona State University

From top right:

- **Alberto Acevedo**, CSU, San Bernardino
- **Craig Thompson**, University of Arizona
- **Brian Bell**, Arizona State University
- **Brian Bollen**, SUNY, Albany

For more information about donating to the
Don Wilson fund, the Michael Tabor Fellowship Endowment,
or the Applied Mathematics General Fund,
please visit the following link:

http://appliedmath.arizona.edu/donate-program-applied-mathematics

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